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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,325	06/27/2007	James Russell	RUSSELL-5	9433

1444 7590 03/16/2010

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
03/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,325	RUSSELL ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-17,24-27,29,30 and 34-36* is/are pending in the application.

4a) Of the above claim(s) *24-27,29,30 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-17* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0806*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a national stage entry of PCT/CA05/00356, filed March 4, 2005, which claims the benefit of US Provisional application 60/549,559, filed March 4, 2004. It is noted that the international search report for PCT/CA/00356 has been received and considered by the examiner. Additionally, applicant has provided an information disclosure statement listing the references cited in the search report, and those references have been considered (see enclosed substitute form 1449/PTO).

2. This action is responsive to the Preliminary Amendment and Response to Restriction Requirement filed December 30, 2009. Claim 3 has been canceled, and claims 1, 10, 13, and 16 have been amended. Claims 24-27, 29-30, and 34-36 have been withdrawn (see below), and claims 1-2 and 4-17 are now under consideration herein.

Election/Restrictions

3. Applicant's election with traverse of Group I in the reply filed on January 14, 2010 is acknowledged. The traversal is on the ground(s) that (a) it would not be unduly burdensome to examine "all three indicated groups together" and/or (b) because the Park reference cited by the examiner "does not provide a basis for disunification" (see further discussion below). Regarding (a), applicant's argument (which is interpreted as referencing Groups I-III based on applicant's initial comments) is not persuasive because burden is not a relevant criterion with respect to restriction/unity of invention determination in a 371 application (see, e.g., MPEP 1893.03(d), which makes clear that restriction practice under 37 CFR 1.141-1.146 is not applicable in a 371 application).

Regarding (b), applicant notes that the claims have been amended to recite 2 particular SNPs, and urges that Park "does not teach that the 1418 SNP has any predictive value for risk of myocardial infarction (let alone any other inflammatory condition". The examiner concurs that Park does not teach or suggest the invention of the claims as they are now amended. However, it is reiterated with regard to Group III that Park et al disclose oligonucleotides meeting the requirements of Group III. Additionally, Groups II and IV continue to broadly encompass determining thrombomodulin genotypes (Group II) and media comprising genotype correlations (Group IV); i.e., Groups II and IV are not limited to specific particular polymorphisms and do not require correlations with those polymorphisms now recited in the claims of Group I. Thus, applicant's arguments are not persuasive.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 24-27, 29-30 and 34-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 30, 2009.

Priority

5. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the

reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional

information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

In the present case, it is further noted that the instant priority claim was granted in the corresponding PCT application as evidenced by the recitation of the priority claim on the first page of WO 2005/085273 A1.

Oath/Declaration

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor.

More particularly, it is noted that each inventor has listed his citizenship as "British Columbia." Although the examiner has considered treating this matter as an informality as a courtesy to applicant, the oath/declaration cannot be accepted because 35 USC 115 explicitly requires that applicant "shall state of what country he is a citizen."

Claim Objections

7. Claim 16 is objected to because of the following informalities: the claim lacks proper punctuation separating each item listed in the claim; see, for example, the recitation "ischemia ischemia...." at lines 5-6, and the list of organs in line 24. Appropriate correction is required. Applicant's attention is also drawn to the rejection of the claim under 35 USC 112, second paragraph set forth below.

Claim Rejections - 35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2, 4, 6-8, and 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 4, and 6-8 are indefinite over the recitation of the limitation "the polymorphic site" in claim 2 (from which claims 4 and 6-8 depend). There is insufficient antecedent basis for this limitation in the claim, as claim 1 as amended no longer references any "polymorphic site(s)".

Claim 4 is indefinite over the recitation of the limitation "the polymorphic site in linkage disequilibrium with position 5318 has a D' value of ≥ 0.8 or r2 value ≥ 0.8".

There is insufficient antecedent basis for this limitation in the claim, as claims 1-2 as amended no longer reference any "polymorphic site in linkage disequilibrium." As a result, it is also further unclear as to how claim 4 might further limit the claims from which it depends (as those claims no longer encompass polymorphic sites in linkage disequilibrium). Because claim 2 (from which claim 4 depends) has been amended to require "position 5318 of SEQ ID NO: 1" and to delete the reference to "a polymorphic site in linkage disequilibrium thereto", claim 4 has been interpreted as for purposes of further consideration herein as being directed to the same invention as claim 2. However, clarification (or cancellation) of claim 4 is required in response to this Office action.

Claim 6 is indefinite over the recitation of the limitation "further comprising determining the thrombomodulin sequence information for the subject". It is unclear what is required by this language. Claims 1-2 (from which claim 6 depends) already require "determining a genotype of said subject" at one of two particular positions in SEQ ID NO: 1, and it is not clear what might constitute "the thrombomodulin sequence information" that must further be determined to meet the requirements of claim 6. Accordingly, clarification is required.

Regarding claims 10-15, the terms "decreased likelihood" in claim 10 (pertinent to claims 10-12), "increased likelihood" in claim 13 (pertinent to claims 13-15), and "less severe" in claim 14 are all relative terms which render the claims indefinite. The term are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. The claims should be amended so as to make clear with respect to what "likelihood" would be considered increased or decreased, and with respect to what a comparison is made in determining "less severe" dysfunction.

Claims 13-15 are indefinite over the recitation of the limitation "the protective genotype" in claim 13 (from which claims 14-15 depend). There is insufficient antecedent basis for this limitation in the claim, as a "protective genotype" is never previously referenced in the claims, as it is unclear what might constitute "the protective genotype" within the context of claim 13.

Claim 16 is indefinite because the wording of the claim is vague and confusing, such that it is unclear what elements/condition are or are not encompassed by the claims. For example, at lines 8-9, the claim includes a recitation "and for patients undergoing major surgery or dialysis....." and a subsequent list of different types of patients. It is unclear whether the remainder of the claim only applies to these particular types of patients, or whether at some point the claim reverts to a generally applicable list of "inflammatory conditions". The claim as written does not clearly apprise one of skill in the art as to what conditions are embraced by or excluded from the claim. Further, the claim references different types of microorganisms in a way suggesting that those organisms themselves (as opposed to infection with such organisms) constitute "inflammatory conditions" (for example, E. coli is a bacterium, not an "inflammatory condition"; note also the reference in the claim to Pneumocystis carinii, Legionella, Epstein-Barr virus, influenza A, etc.). Further, the phrase "such as" (see line 26)

renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 1-2, 4-6, and 9-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to a method "for obtaining a prognosis for a subject having, or at risk of developing, an inflammatory condition." The method of independent claim 1 comprises a single step of "determining a genotype of said subject at position 5318 or at position 4007 of SEQ ID NO: 1, wherein said genotype is indicative of an ability of the subject to recover from the inflammatory condition". Two dependent claims included in this rejection recite additional steps: claim 5 requires "comparing" the determined genotype with known genotypes, and claim 6 requires "determining the thrombomodulin sequence information for the subject". Claim 9 further provides a list of various techniques that may be used to accomplish 'determining" of genotype, which list includes an option of "reading sequence data" (as well as other alternatives that require manipulative steps). It is also noted that dependent claims 7-8, which are not rejected herein, recite further limitations requiring that the determining of the claims be "performed on a nucleic acid sample from the subject" (claim 7) and further that a nucleic acid sample be obtained from the subject (claim 8). Thus, the text of claims 7-8, as well as of claim 9, indicates that claim 1 does not require any physical use or

manipulation of a subject's nucleic acid, but rather that claim 1 embraces non-manipulative steps such as merely reading or otherwise ascertaining the identity of a subject's genotype without in fact performing any active or manipulative steps to accomplish "determining".

The claims have been evaluated in accordance with the "Interim examination instructions for evaluating subject matter eligibility under 35 USC 101" (posted August 27, 2009 at www.uspto.gov; hereinafter "the Instructions"). The instant claims are directed to a process, i.e., a series of steps or acts to be performed. As discussed in the Instructions, and based on Supreme Court precedent (*Diamond v. Diehr*, 450 US 175, 184 (1981); *Parker v. Flook*, 437 US 584, 588 n.9 (1978); *Gottschalk v. Benson*, 409 US 63, 70 (1972); *Cochrane v. Deener*, 94 US 780, 787-88 (1876)) and *In re Bilski* (545 F.3d 943, 88 USPQ2d 1385 (Fed. Cir. 2008)), in order for such a claim to qualify as a patent-eligible process claim, the claimed method must (1) be tied to a particular machine or apparatus, or (2) transform a particular article to a different state or thing, i.e., the claim must pass the "machine-or-transformation test". Additionally, the machine or transformation (**if present**) (a) must impose meaningful limits on the method claim's scope, and (b) cannot merely be recited in an insignificant step such as data gathering or outputting; i.e., insignificant extra-solution activity cannot transform an unpatentable principle into a patentable process (*Bilski*).

In the instant case, the methods of the rejected claims are not patent-eligible because they fail the "machine-or-transformation test". First, the claims are not tied in any way to a particular machine or apparatus (i.e., do not meet (1), above). Second,

the claims do not require a transformation of an article to a different state or thing (such that the claims do not meet (2), above). More particularly, the claims, as is discussed above, clearly encompass "determining" genotype in such a way that no transformation of any article of any kind actually occurs. In view of claim 9, as well as applicant's discussion of genotype "determining" in the specification (at, e.g., page 9), one of skill in the art would recognize that this term may embrace activities that are manipulative/transformative (such as the various nucleic acid assays of claim 9), as well as activities that are not (e.g., reading, reviewing or interpreting data/sequence information to "determine" whether a particular subject does or does not have a particular genotype, such that no actual physical or manipulative steps are required). While the "determining" of the instant claims broadly encompasses methods involving physical manipulations in which the particular nucleotides of claim 1 are determined in an actual nucleic acid sample to achieve the objective of "obtaining a prognosis" (see again dependent claims 7-8), the Instructions make clear that claims that embrace both statutory and non-statutory embodiments must be rejected under 35 USC 101 as being directed to non-statutory subject matter. As such, claims 1-2, 4-6, and 9-17 do not qualify as patent-eligible process claims. Regarding claim 5, the "comparing" of claim 5 does not require any type of physical manipulation, and therefore similarly fails both elements of the "machine or transformation" test. With further regard to claim 6, the 'determining' of that claim also encompasses both manipulative and non-manipulative "determining," and therefore must also be rejected as directed to non-statutory subject

matter. With further regard to dependent claim 9, it is noted that this rejection particularly applies to embodiment (i) of that claim.

Claim Rejections - 35 USC § 112, first paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-2 and 4-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)). It is noted that the examiner has considered all of the evidence related to each of these factors, and that

those factors, reasons and evidence that have led to a conclusion that enablement is lacking are discussed below (*MPEP* 2164.04).

The claims are directed to a method "for obtaining a prognosis for a subject having, or at risk of developing, an inflammatory condition." The method of independent claim 1 (from which all claims depend) comprises a single step of "determining a genotype of said subject at position 5318 or at position 4007 of SEQ ID NO: 1, wherein said genotype is indicative of an ability of the subject to recover from the inflammatory condition". Thus, enablement of the claimed invention requires that a genotype as determined in claim 1 allow one to obtain a prognosis for an "inflammatory condition". It is noted that dependent claims 10-15 recite further characteristics of risk/protective genotypes and their relationships with particular conditions, and further that claims 16-17 further define/describe an "inflammatory condition;" claim 16 in particular makes clear the vast and disparate types of conditions that are embraced by the term "inflammatory condition". It is also noted, however, that the specification explicitly excludes "myocardial infarction" from being considered an "inflammatory condition" embraced by the claims (see page 9, lines 6-7 of the specification).

The specification discloses that position 4007 of SEQ ID NO: 1 corresponds to a thrombomodulin gene polymorphism that is well-known in the art, C1418T (see, e.g., pages 3-4 of the specification; see also the discussion of prior art, below). The specification acknowledges that prior art findings with regard to associations between the C1418T polymorphism and "various thrombotic events and cardiovascular disease" have been inconsistent and "uncertain" (page 4, final paragraph). At pages 5-6 of the

specification, applicants teach that their own assays were conducted on haplotypes including a polymorphism at position 5318 of SEQ ID NO: 1, which polymorphism is disclosed as being in linkage disequilibrium with the position 4007 polymorphism (see bottom of page 6). At page 7, applicants disclose that the "risk genotype" of the invention "may include at least one A nucleotide at position 5318 or at least one C nucleotide at position 4007 of SEQ ID NO: 1". These "risk" genotypes are reiterated page, e.g., pages 11-12 of the specification, at which time applicants also disclose genotypes including 5318C and/or 4007T as "protective" genotypes. Thus, applicants disclose that they consider the C allele of the known C1418T variant to be associated with risk of poor outcome/poor prognosis. Linkage of the 4007 and 5318 polymorphisms was determined via prior art methods as disclosed at page 38 and 40-41 (see also Figure 1), and applicants report that they genotyped 3 SNPs (including 5318 and 2 others) in performing their analyses of patient outcome. At pages 8-9 applicants recite a vast number of different "inflammatory conditions" that are embraced by the claims (see also claim 16), which list explicitly excludes "myocardial infarction" (as noted above).

It is unpredictable as to whether one of skill in the relevant art could actually practice the methods claimed herein by applicants. Applicants report the successful genotyping and analysis of a group of 223 Caucasian patients with at least 2 of 4 SIRS criteria (see, e.g., pages 41-42). The specification reports that haplotypes including 5318C were found to be "protective," while individuals possessing the 5318A allele were found to be "1.95 times more likely to have a poor outcome....after adjusting for gender,

age, and surgical diagnosis". The specification also provides a separate analysis of the 5318 allele, reporting again that the C allele "appeared to be associated" with lower 28 day mortality (referencing Fig 3), and that the 5318A allele was also found to be significantly associated with 28 day mortality in a subgroup of the SIRS patients that had sepsis or septic shock (lines 15-22; Fig 5). The specification also reports that in the larger 223 patient cohort, as well as in the sepsis subgroup, the 5318A allele was associated with a more vigorous inflammatory response and fewer days alive and free (DAF) of different SIRS criteria (page 43, lines 24-34). At page 44, lines 1-14, the specification also reports an association between the "protective" 5318C allele and fewer DAF of cardiovascular failure and vasopressors, referencing Figure 6 (although Figure 6 itself appears to contradict these statements). Page 44 also reports associations between the 5318A and fewer DAF of respiratory failure, ventilation, hematologic system failure, neurologic dysfunction, and hepatic dysfunction. However, the specification also then states that "When analyzed individually, there were no significant associations" between A5318C and "28-day mortality or multiple organ system failure" (lines 13-14). Thus, the specification reports limited and contradictory findings with regard to one small group of human subjects exhibiting SIRS, a subset of whom have sepsis. For example, the specification contains contradictory statements with respect to whether a 5318 allele is or is not associated with 28 day mortality in this population, and is also contradictory with regard to an association between the C allele and cardiovascular failure. Additionally, the specification is silent with regard to any evidence of associations between either allele of the claims and the vast majority of

inflammatory conditions embraced by the claims in any type of subject. The specification does not report replication of any of applicant's findings in any other population, and such replication is considered in the relevant art to be a standard step that should be taken before concluding that any association of the type claimed herein is significant (see, e.g., Dahlman et al, Nature Genetics 30:149-150 [Feb 2002]). Additionally, the prior art as exemplified by Dahlman et al teaches that the number of subjects assayed by applicants is inadequate to conclude that a true genetic association is present (see entire reference). Accordingly, given the guidance provided in the specification, in view of the state of the art at the time the invention was made, one of skill in the relevant art would not conclude that the claims under consideration herein are in fact enabled. Lacking guidance of the specification, one of skill in the art may look to the teachings of the prior art for further guidance with regard to enablement of a claimed invention. However, in the instant case, the prior art does not provide any supplementary enabling guidance with regard to the instantly claimed invention. The prior art is silent with regard to any established correlations between the polymorphism applicant references as position 5318 of SEQ ID NO: 1 and any prognosis for any "inflammatory condition" embraced by the claims. Regarding the 4007 polymorphism with which the 5318 polymorphism is linked (and which is separately embraced by the claims), the prior art provides contradictory findings that would not allow a skilled artisan to draw the conclusion that any embodiments embraced by the claims may be successfully practiced. For example, although it is noted that MI is not embraced by the claims, the prior art as exemplified by Konstantoulas et al (Thrombosis and

Haemostasis 91:628-30 [March 2004]; cited in IDS) summarizes the state of the art with regard to the C1418T thrombomodulin polymorphism and MI risk at the time applicant's invention was made, stating that "both or neither" variant have been reported to have an MI association in the prior art (see page 628, left column). Thus, the teachings of Konstantoulas et al make clear that findings reported when attempting to assay the significance of this particular polymorphism with respect to another disease/condition have been confusing and contradictory (in confirmation of applicant's own teachings in the specification regarding the state of the art). Additionally, Aleksic et al (Journal of Thrombosis and Haemostasis 1:88-94 [Jan 2003]; cited herein), assaying a much larger group of cases and controls than applicant, reported a failure to associate either allele of the 1418 polymorphism with venous thromboembolism or thrombosis (see entire reference). Accordingly, the teachings of the prior art do not support enablement of applicant's claims, and further indicate that prior art studies of the 1418 polymorphism have produced conflicting results, indicating a particular need to replicate any findings before drawing conclusions regarding associations between this polymorphism and any disease/condition or patient prognosis. Given the high level of skill of one skilled in the relevant art, it is clearly within the ability of such an artisan to undertake further experimentation aimed at determining, e.g., whether any actual correlations or associations between either of the alleles embraced by the claims and various types of "inflammatory conditions" exist. However, the outcome of such experimentation is completely unpredictable, and given the absence of evidence at the time the invention was made that any such associations actually exist, it is possible that even an infinite

quantity of experimentation would not result in enablement of any methods embraced by the present claims. As such a type and quantity of experimentation is clearly undue, enablement is lacking with regard to the claimed invention. Additionally, given the lack of enablement with respect to preferred subjects (humans) and preferred conditions embraced by the claims (SIRS, sepsis), enablement is also clearly lacking with regard to the numerous other types of subjects and conditions embraced by the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 8:30 am-2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571/272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634